



SEQUENCE LISTING

<110> BROWN, ARTHUR M.
WIBLE, BARBARA A.

<120> METHODS OF INDUCING APOPTOSIS IN HYPERPROLIFERATION
CELLS

<130> 22884/04085

<140> 10/784,528

<141> 2004-02-23

<150> 10/000,778

<151> 2001-10-31

<160> 10

<170> PatentIn Ver. 3.3

<210> 1

<211> 1725

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(1722)

<400> 1

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| Met Lys Ile Lys Glu Leu Tyr Arg Arg Arg Phe Pro Arg Lys Thr Leu | |
| 1 5 10 15 | |
| ggg ccc tct gat ctg tcc ctt ctg tct ttg ccc cct ggc acc tct cct | 96 |
| Gly Pro Ser Asp Leu Ser Leu Leu Ser Leu Pro Pro Gly Thr Ser Pro | |
| 20 25 30 | |
| gta ggc tcc cct ggt cct cta gct ccc att ccc cca acg ctg ttg gcc | 144 |
| Val Gly Ser Pro Gly Pro Leu Ala Pro Ile Pro Pro Thr Leu Leu Ala | |
| 35 40 45 | |
| cct ggc acc ctg ctg ggc ccc aag cgt gag gtg gac atg cac ccc cct | 192 |
| Pro Gly Thr Leu Leu Gly Pro Lys Arg Glu Val Asp Met His Pro Pro | |
| 50 55 60 | |
| ctg ccc cag cct gtg cac cct gat gtc acc atg aaa cca ttg ccc ttc | 240 |
| Leu Pro Gln Pro Val His Pro Asp Val Thr Met Lys Pro Leu Pro Phe | |
| 65 70 75 80 | |
| tat gaa gtc tat ggg gag ctg atc cgg ccc acc acc ctt gca tcc act | 288 |
| Tyr Glu Val Tyr Gly Glu Leu Ile Arg Pro Thr Thr Leu Ala Ser Thr | |
| 85 90 95 | |
| tct agc cag cgg ttt gag gaa gcg cac ttt acc ttt gcc ctg aca ccc | 336 |
| Ser Ser Gln Arg Phe Glu Glu Ala His Phe Thr Phe Ala Leu Thr Pro | |
| 100 105 110 | |

| | |
|---|------|
| cag caa gtg cag cag att ctt aca tcc aga gag gtt ctg cca gga gcc | 384 |
| Gln Gln Val Gln Gln Ile Leu Thr Ser Arg Glu Val Leu Pro Gly Ala | |
| 115 120 125 | |
| aaa tgt gat tat acc ata cag gtg cag cta agg ttc tgt ctc tgt gag | 432 |
| Lys Cys Asp Tyr Thr Ile Gln Val Gln Leu Arg Phe Cys Leu Cys Glu | |
| 130 135 140 | |
| acc agc tgc ccc cag gaa gat tat ttt ccc ccc aac ctc ttt gtc aag | 480 |
| Thr Ser Cys Pro Gln Glu Asp Tyr Phe Pro Pro Asn Leu Phe Val Lys | |
| 145 150 155 160 | |
| gtt aat ggg aaa ctg tgc ccc ctg ccg ggt tac ctt ccc cca acc aag | 528 |
| Val Asn Gly Lys Leu Cys Pro Leu Pro Gly Tyr Leu Pro Pro Thr Lys | |
| 165 170 175 | |
| aat ggg gcc gag ccc aag agg ccc agc cgc ccc atc aac atc aca ccc | 576 |
| Asn Gly Ala Glu Pro Lys Arg Pro Ser Arg Pro Ile Asn Ile Thr Pro | |
| 180 185 190 | |
| ctg gct cga ctc tca gcc act gtt ccc aac acc att gtg gtc aat tgg | 624 |
| Leu Ala Arg Leu Ser Ala Thr Val Pro Asn Thr Ile Val Val Asn Trp | |
| 195 200 205 | |
| tca tct gag ttc gga cgg aat tac tcc ttg tct gtg tac ctg gtg agg | 672 |
| Ser Ser Glu Phe Gly Arg Asn Tyr Ser Leu Ser Val Tyr Leu Val Arg | |
| 210 215 220 | |
| cag ttg act gca gga acc ctt cta caa aaa ctc aga gca aag ggt atc | 720 |
| Gln Leu Thr Ala Gly Thr Leu Leu Gln Lys Leu Arg Ala Lys Gly Ile | |
| 225 230 235 240 | |
| cgg aac cca gac cac tcg cgg gca ctg atc aag gag aaa ttg act gct | 768 |
| Arg Asn Pro Asp His Ser Arg Ala Leu Ile Lys Glu Lys Leu Thr Ala | |
| 245 250 255 | |
| gac cct gac agt gag gtg gcc act aca agt ctc cgg gtg tca ctc atg | 816 |
| Asp Pro Asp Ser Glu Val Ala Thr Thr Ser Leu Arg Val Ser Leu Met | |
| 260 265 270 | |
| tgc ccg cta ggg aag atg cgc ctg act gtc cct tgt cgt gcc ctc acc | 864 |
| Cys Pro Leu Gly Lys Met Arg Leu Thr Val Pro Cys Arg Ala Leu Thr | |
| 275 280 285 | |
| tgt gcc cac ctg cag agc ttc gat gct gcc ctt tat cta cag atg aat | 912 |
| Cys Ala His Leu Gln Ser Phe Asp Ala Ala Leu Tyr Leu Gln Met Asn | |
| 290 295 300 | |
| gag aag aag cct aca tgg aca tgt cct gtg tgt gac aag aag gct ccc | 960 |
| Glu Lys Lys Pro Thr Trp Thr Cys Pro Val Cys Asp Lys Lys Ala Pro | |
| 305 310 315 320 | |
| tat gaa tct ctt atc att gat ggt tta ttt atg gag att ctt agt tcc | 1008 |
| Tyr Glu Ser Leu Ile Ile Asp Gly Leu Phe Met Glu Ile Leu Ser Ser | |
| 325 330 335 | |

| | | | | | |
|-------------|---------------------|-----------------|-----------------|-------------|------|
| tgt tca gat | tgt gat gag atc | caa ttc atg | gaa gat gga | tcc tgg tgc | 1056 |
| Cys Ser Asp | Cys Asp Glu Ile Gln | Phe Met Glu Asp | Gly Ser Trp Cys | | |
| 340 | 345 | 350 | | | |
| cca atg aaa | ccc aag aag gag | gca tct gag | gtt tgc ccc | ccg cca ggg | 1104 |
| Pro Met Lys | Pro Lys Lys Glu | Ala Ser Glu Val | Cys Pro Pro | Pro Gly | |
| 355 | 360 | 365 | | | |
| tat ggg ctg | gat ggc ctc | cag tac agc | cca gtc cag | ggg gga gat | 1152 |
| Tyr Gly Leu | Asp Gly Leu Gln | Tyr Ser Pro Val | Gln Gly Gly | Asp Pro | |
| 370 | 375 | 380 | | | |
| tca gag aat | aag aag aag gtc | gaa gtt att | gac ttg aca | ata gaa agc | 1200 |
| Ser Glu Asn | Lys Lys Lys Val | Glu Val Ile Asp | Leu Thr Ile | Glu Ser | |
| 385 | 390 | 395 | | 400 | |
| tca tca gat | gag gag gat | ctg ccc cct | acc aag aag | cac tgt tct | 1248 |
| Ser Ser Asp | Glu Glu Asp Leu | Pro Pro Thr | Lys Lys His | Cys Ser Val | |
| 405 | 410 | 415 | | | |
| acc tca gct | gcc atc ccg | gcc cta cct | gga agc aaa | gga gtc ctg | 1296 |
| Thr Ser Ala | Ala Ile Pro Ala | Leu Pro Gly | Ser Lys Gly | Val Leu Thr | |
| 420 | 425 | 430 | | | |
| tct ggc cac | cag cca tcc | tcg gtg cta | agg agc cct | gct atg ggc | 1344 |
| Ser Gly His | Gln Pro Ser Ser | Val Leu Arg Ser | Pro Ala Met | Gly Thr | |
| 435 | 440 | 445 | | | |
| ttg ggt ggg | gat ttc ctg | tcc agt ctc | cca cta cat | gag tac cca | 1392 |
| Leu Gly Gly | Asp Phe Leu Ser | Leu Pro Leu His | Glu Tyr Pro | Pro Pro | |
| 450 | 455 | 460 | | | |
| gcc ttc cca | ctg gga gcc | gac atc caa | ggg tta gat | tta ttt tca | 1440 |
| Ala Phe Pro | Leu Gly Ala Asp | Ile Gln Gly | Leu Asp Leu | Phe Ser Phe | |
| 465 | 470 | 475 | | 480 | |
| ctt cag aca | gag agt cag | cac tat ggc | ccc tct gtc | atc acc tca | 1488 |
| Leu Gln Thr | Glu Ser Gln His | Tyr Gly Pro | Ser Val Ile | Thr Ser Leu | |
| 485 | 490 | 495 | | | |
| gat gaa cag | gat gcc ctt | ggc cac ttc | ttc cag tac | cga ggg acc | 1536 |
| Asp Glu Gln | Asp Ala Leu Gly | His Phe Phe | Gln Tyr Arg | Gly Thr Pro | |
| 500 | 505 | 510 | | | |
| tct cac ttt | ctg ggc cca | ctg gcc ccc | acg ctg ggg | agc tcc cac | 1584 |
| Ser His Phe | Leu Gly Pro Leu | Ala Pro Thr | Leu Gly Ser | Ser His Cys | |
| 515 | 520 | 525 | | | |
| agc gcc act | ccg gcg ccc | cct cct ggc | cgt gtc agc | agc att gtg | 1632 |
| Ser Ala Thr | Pro Ala Pro Pro | Pro Gly Arg | Val Ser Ser | Ile Val Ala | |
| 530 | 535 | 540 | | | |
| cct ggg ggg | gcc ttg agg | gag ggg cat | gga gga ccc | ctg ccc tca | 1680 |
| Pro Gly Gly | Ala Leu Arg Glu | Gly Gly His | Gly Gly Pro | Leu Pro Ser | |
| 545 | 550 | 555 | | 560 | |

ccc tct ttg act ggc tgt cgg tca gac atc att tcc ctg gac tga 1725
 Pro Ser Leu Thr Gly Cys Arg Ser Asp Ile Ile Ser Leu Asp
 565 570

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 <212> PRT
 <213> Homo sapiens

<400> 2
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 20 25 30
 Val Gly Ser Pro Gly Pro Leu Ala Pro Ile Pro Pro Thr Leu Leu Ala
 35 40 45
 Pro Gly Thr Leu Leu Gly Pro Lys Arg Glu Val Asp Met His Pro Pro
 50 55 60
 Leu Pro Gln Pro Val His Pro Asp Val Thr Met Lys Pro Leu Pro Phe
 65 70 75 80
 Tyr Glu Val Tyr Gly Glu Leu Ile Arg Pro Thr Thr Leu Ala Ser Thr
 85 90 95
 Ser Ser Gln Arg Phe Glu Glu Ala His Phe Thr Phe Ala Leu Thr Pro
 100 105 110
 Gln Gln Val Gln Gln Ile Leu Thr Ser Arg Glu Val Leu Pro Gly Ala
 115 120 125
 Lys Cys Asp Tyr Thr Ile Gln Val Gln Leu Arg Phe Cys Leu Cys Glu
 130 135 140
 Thr Ser Cys Pro Gln Glu Asp Tyr Phe Pro Pro Asn Leu Phe Val Lys
 145 150 155 160
 Val Asn Gly Lys Leu Cys Pro Leu Pro Gly Tyr Leu Pro Pro Thr Lys
 165 170 175
 Asn Gly Ala Glu Pro Lys Arg Pro Ser Arg Pro Ile Asn Ile Thr Pro
 180 185 190
 Leu Ala Arg Leu Ser Ala Thr Val Pro Asn Thr Ile Val Val Asn Trp
 195 200 205
 Ser Ser Glu Phe Gly Arg Asn Tyr Ser Leu Ser Val Tyr Leu Val Arg
 210 215 220
 Gln Leu Thr Ala Gly Thr Leu Leu Gln Lys Leu Arg Ala Lys Gly Ile
 225 230 235 240
 Arg Asn Pro Asp His Ser Arg Ala Leu Ile Lys Glu Lys Leu Thr Ala
 245 250 255

Asp Pro Asp Ser Glu Val Ala Thr Thr Ser Leu Arg Val Ser Leu Met
 260 265 270
 Cys Pro Leu Gly Lys Met Arg Leu Thr Val Pro Cys Arg Ala Leu Thr
 275 280 285
 Cys Ala His Leu Gln Ser Phe Asp Ala Ala Leu Tyr Leu Gln Met Asn
 290 295 300
 Glu Lys Lys Pro Thr Trp Thr Cys Pro Val Cys Asp Lys Lys Ala Pro
 305 310 315 320
 Tyr Glu Ser Leu Ile Ile Asp Gly Leu Phe Met Glu Ile Leu Ser Ser
 325 330 335
 Cys Ser Asp Cys Asp Glu Ile Gln Phe Met Glu Asp Gly Ser Trp Cys
 340 345 350
 Pro Met Lys Pro Lys Lys Glu Ala Ser Glu Val Cys Pro Pro Pro Gly
 355 360 365
 Tyr Gly Leu Asp Gly Leu Gln Tyr Ser Pro Val Gln Gly Gly Asp Pro
 370 375 380
 Ser Glu Asn Lys Lys Lys Val Glu Val Ile Asp Leu Thr Ile Glu Ser
 385 390 395 400
 Ser Ser Asp Glu Glu Asp Leu Pro Pro Thr Lys Lys His Cys Ser Val
 405 410 415
 Thr Ser Ala Ala Ile Pro Ala Leu Pro Gly Ser Lys Gly Val Leu Thr
 420 425 430
 Ser Gly His Gln Pro Ser Ser Val Leu Arg Ser Pro Ala Met Gly Thr
 435 440 445
 Leu Gly Gly Asp Phe Leu Ser Ser Leu Pro Leu His Glu Tyr Pro Pro
 450 455 460
 Ala Phe Pro Leu Gly Ala Asp Ile Gln Gly Leu Asp Leu Phe Ser Phe
 465 470 475 480
 Leu Gln Thr Glu Ser Gln His Tyr Gly Pro Ser Val Ile Thr Ser Leu
 485 490 495
 Asp Glu Gln Asp Ala Leu Gly His Phe Phe Gln Tyr Arg Gly Thr Pro
 500 505 510
 Ser His Phe Leu Gly Pro Leu Ala Pro Thr Leu Gly Ser Ser His Cys
 515 520 525
 Ser Ala Thr Pro Ala Pro Pro Pro Gly Arg Val Ser Ser Ile Val Ala
 530 535 540
 Pro Gly Gly Ala Leu Arg Glu Gly His Gly Gly Pro Leu Pro Ser Gly
 545 550 555 560

Pro Ser Leu Thr Gly Cys Arg Ser Asp Ile Ile Ser Leu Asp
 565 570

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 <211> 28
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic
 peptide

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Thr Leu Leu Gly Pro Lys Arg Glu Val Asp Met His
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<210> 4
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic
 peptide

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<210> 5
 <211> 650
 <212> PRT
 <213> Homo sapiens

<400> 5
 Met Ala Asp Ser Ala Glu Leu Lys Gln Met Val Met Ser Leu Arg Val
 1 5 10 15

Ser Glu Leu Gln Val Leu Leu Gly Tyr Ala Gly Arg Asn Lys His Gly
 20 25 30

Arg Lys His Glu Leu Leu Thr Lys Ala Leu His Leu Leu Lys Ala Gly
 35 40 45

Cys Ser Pro Ala Val Gln Met Lys Ile Lys Glu Leu Tyr Arg Arg Arg
 50 55 60

Phe Pro Gln Lys Ile Met Thr Pro Ala Asp Leu Ser Ile Pro Asn Val
 65 70 75 80

Leu Ile Ile Asp Gly Leu Phe Met Glu Ile Leu Lys Tyr Cys Thr Asp
 385 390 395 400
 Cys Asp Glu Ile Gln Phe Lys Glu Asp Gly Thr Trp Ala Pro Met Arg
 405 410 415
 Ser Lys Lys Glu Val Gln Glu Val Ser Ala Ser Tyr Asn Gly Val Asp
 420 425 430
 Gly Cys Leu Ser Ser Thr Leu Glu His Gln Val Ala Ser His His Gln
 435 440 445
 Ser Ser Asn Lys Asn Lys Lys Val Glu Val Ile Asp Leu Thr Ile Asp
 450 455 460
 Ser Ser Ser Asp Glu Glu Glu Glu Glu Pro Ser Ala Lys Arg Thr Cys
 465 470 475 480
 Pro Ser Leu Ser Pro Thr Ser Pro Leu Asn Asn Lys Gly Ile Leu Ser
 485 490 495
 Leu Pro His Gln Ala Ser Pro Val Ser Arg Thr Pro Ser Leu Pro Ala
 500 505 510
 Val Asp Thr Ser Tyr Ile Asn Thr Ser Leu Ile Gln Asp Tyr Arg His
 515 520 525
 Pro Phe His Met Thr Pro Met Pro Tyr Asp Leu Gln Gly Leu Asp Phe
 530 535 540
 Phe Pro Phe Leu Ser Gly Asp Asn Gln His Tyr Asn Thr Ser Leu Leu
 545 550 555 560
 Ala Ala Ala Ala Ala Val Ser Asp Asp Gln Asp Leu Leu His Ser
 565 570 575
 Ser Arg Phe Phe Pro Tyr Thr Ser Ser Gln Met Phe Leu Asp Gln Leu
 580 585 590
 Ser Ala Gly Gly Ser Thr Ser Leu Pro Thr Thr Asn Gly Ser Ser Ser
 595 600 605
 Gly Ser Asn Ser Ser Leu Val Ser Ser Asn Ser Leu Arg Glu Ser His
 610 615 620
 Ser His Thr Val Thr Asn Arg Ser Ser Thr Asp Thr Ala Ser Ile Phe
 625 630 635 640
 Gly Ile Ile Pro Asp Ile Ile Ser Leu Asp
 645 650

<210> 6

<211> 651

<212> PRT

<213> Mus musculus

<400> 6

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Asp | Ser | Ala | Glu | Leu | Lys | Gln | Met | Val | Met | Ser | Leu | Arg | Val |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Ser | Glu | Leu | Gln | Val | Leu | Leu | Gly | Tyr | Ala | Gly | Arg | Asn | Lys | His | Gly |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Arg | Lys | His | Glu | Leu | Leu | Thr | Lys | Ala | Leu | His | Leu | Leu | Lys | Ala | Gly |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Cys | Ser | Pro | Ala | Val | Gln | Met | Lys | Ile | Lys | Glu | Leu | Tyr | Arg | Arg | Arg |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Phe | Pro | Gln | Lys | Ile | Met | Thr | Pro | Ala | Asp | Leu | Ser | Ile | Pro | Asn | Val |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| His | Ser | Ser | Pro | Met | Pro | Pro | Thr | Leu | Ser | Pro | Ser | Thr | Ile | Pro | Gln |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Leu | Thr | Tyr | Asp | Gly | His | Pro | Ala | Ser | Ser | Pro | Leu | Leu | Pro | Val | Ser |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Leu | Leu | Gly | Pro | Lys | His | Glu | Leu | Glu | Leu | Pro | His | Leu | Thr | Ser | Ala |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| Leu | His | Pro | Val | His | Pro | Asp | Ile | Lys | Leu | Gln | Lys | Leu | Pro | Phe | Tyr |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Asp | Leu | Leu | Asp | Glu | Leu | Ile | Lys | Pro | Thr | Ser | Leu | Ala | Ser | Asp | Asn |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Ser | Gln | Arg | Phe | Arg | Glu | Thr | Cys | Phe | Ala | Phe | Ala | Leu | Thr | Pro | Gln |
| | | | | 165 | | | | | 170 | | | | | 175 | |
| Gln | Val | Gln | Gln | Ile | Ser | Ser | Ser | Met | Asp | Ile | Ser | Gly | Thr | Lys | Cys |
| | | | 180 | | | | | 185 | | | | | 190 | | |
| Asp | Phe | Thr | Val | Gln | Val | Gln | Leu | Arg | Phe | Cys | Leu | Ser | Glu | Thr | Ser |
| | | 195 | | | | | 200 | | | | | 205 | | | |
| Cys | Pro | Gln | Glu | Asp | His | Phe | Pro | Pro | Asn | Leu | Cys | Val | Lys | Val | Asn |
| | 210 | | | | | 215 | | | | | 220 | | | | |
| Thr | Lys | Pro | Cys | Ser | Leu | Pro | Gly | Tyr | Leu | Pro | Pro | Thr | Lys | Asn | Gly |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| Val | Glu | Pro | Lys | Arg | Pro | Ser | Arg | Pro | Ile | Asn | Ile | Thr | Ser | Leu | Val |
| | | | | 245 | | | | | 250 | | | | | 255 | |
| Arg | Leu | Ser | Thr | Thr | Val | Pro | Asn | Thr | Ile | Val | Val | Ser | Trp | Thr | Ala |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| Glu | Ile | Gly | Arg | Asn | Tyr | Ser | Met | Ala | Val | Tyr | Leu | Val | Lys | Gln | Leu |
| | | 275 | | | | | 280 | | | | | 285 | | | |
| Ser | Ser | Thr | Val | Leu | Leu | Gln | Arg | Leu | Arg | Ala | Lys | Gly | Ile | Arg | Asn |
| | 290 | | | | | 295 | | | | | 300 | | | | |

Pro Asp His Ser Arg Ala Leu Ile Lys Glu Lys Leu Thr Ala Asp Ser
 305 310 315 320
 Asp Ser Glu Ile Ala Thr Thr Ser Leu Arg Val Ser Leu Leu Cys Pro
 325 330 335
 Leu Gly Lys Met Arg Leu Thr Ile Pro Cys Arg Ala Leu Thr Cys Ser
 340 345 350
 His Leu Gln Cys Phe Asp Ala Thr Leu Tyr Ile Gln Met Asn Glu Lys
 355 360 365
 Lys Pro Thr Trp Val Cys Pro Val Cys Asp Lys Lys Ala Pro Tyr Glu
 370 375 380
 His Leu Ile Ile Asp Gly Leu Phe Met Glu Ile Leu Lys Tyr Cys Thr
 385 390 395 400
 Asp Cys Asp Glu Ile Gln Phe Lys Glu Asp Gly Ser Trp Ala Pro Met
 405 410 415
 Arg Ser Lys Lys Glu Val Gln Glu Val Thr Ala Ser Tyr Asn Gly Val
 420 425 430
 Asp Gly Cys Leu Ser Ser Thr Leu Glu His Gln Val Ala Ser His Asn
 435 440 445
 Gln Ser Ser Asn Lys Asn Lys Lys Val Glu Val Ile Asp Leu Thr Ile
 450 455 460
 Asp Ser Ser Ser Asp Glu Glu Glu Glu Glu Pro Pro Ala Lys Arg Thr
 465 470 475 480
 Cys Pro Ser Leu Ser Pro Thr Ser Pro Leu Ser Asn Lys Gly Ile Leu
 485 490 495
 Ser Leu Pro His Gln Ala Ser Pro Val Ser Arg Thr Pro Ser Leu Pro
 500 505 510
 Ala Val Asp Thr Ser Tyr Ile Asn Thr Ser Leu Ile Gln Asp Tyr Arg
 515 520 525
 His Pro Phe His Met Thr Pro Met Pro Tyr Asp Leu Gln Gly Leu Asp
 530 535 540
 Phe Phe Pro Phe Leu Ser Gly Asp Asn Gln His Tyr Asn Thr Ser Leu
 545 550 555 560
 Leu Ala Ala Ala Ala Ala Val Ser Asp Asp Gln Asp Leu Leu His
 565 570 575
 Ser Ser Arg Phe Phe Pro Tyr Thr Ser Ser Gln Met Phe Leu Asp Gln
 580 585 590
 Leu Ser Ala Gly Gly Ser Thr Ser Leu Pro Ala Thr Asn Gly Ser Ser
 595 600 605

Ser Gly Ser Asn Ser Ser Leu Val Ser Ser Asn Ser Leu Arg Glu Ser
 610 615 620

His Gly His Gly Val Ala Ser Arg Ser Ser Ala Asp Thr Ala Ser Ile
 625 630 635 640

Phe Gly Ile Ile Pro Asp Ile Ile Ser Leu Asp
 645 650

<210> 7

<211> 583

<212> PRT

<213> Mus musculus

<400> 7

Met Val Met Ser Phe Arg Val Ser Glu Leu Gln Val Leu Leu Gly Phe
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Ala Gly Arg Asn Lys Ser Gly Arg Lys His Glu Leu Leu Ala Lys Ala
 20 25 30

Leu His Leu Leu Lys Ser Ser Cys Ala Pro Ser Val Gln Met Lys Ile
 35 40 45

Lys Glu Leu Tyr Arg Arg Arg Phe Pro Arg Lys Thr Leu Gly Pro Ser
 50 55 60

Asp Leu Ser Leu Leu Ser Leu Pro Pro Gly Thr Ser Pro Pro Val His
 65 70 75 80

Pro Asp Val Thr Met Lys Pro Leu Pro Phe Tyr Glu Val Tyr Gly Glu
 85 90 95

Leu Ile Arg Pro Thr Thr Leu Ala Ser Thr Ser Ser Gln Arg Phe Glu
 100 105 110

Glu Ala His Phe Thr Phe Ala Leu Thr Pro Gln Gln Leu Gln Gln Ile
 115 120 125

Leu Thr Ser Arg Glu Val Leu Pro Gly Ala Lys Cys Asp Tyr Thr Ile
 130 135 140

Gln Val Gln Leu Arg Phe Cys Leu Cys Glu Thr Ser Cys Pro Gln Glu
 145 150 155 160

Asp Tyr Phe Pro Pro Asn Leu Phe Val Lys Val Asn Gly Lys Leu Cys
 165 170 175

Pro Leu Pro Gly Tyr Leu Pro Pro Thr Lys Asn Gly Ala Glu Pro Arg
 180 185 190

Gly Pro Ala Val Arg Ser Thr Ser His Pro Trp Leu Asp Ser Gln Pro
 195 200 205

Leu Ser Pro Thr Pro Ser Leu Leu Ile Gly His Leu Ser Leu Asp Gly
 210 215 220

| | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Thr | Pro | Cys | Pro | Cys | Leu | Val | Arg | Gln | Leu | Thr | Ala | Gly | Thr | Leu | 225 | 230 | 235 | 240 |
| Leu | Gln | Lys | Leu | Arg | Ala | Lys | Gly | Ile | Arg | Asn | Pro | Asp | His | Ser | Arg | 245 | 250 | 255 | |
| Ala | Leu | Ile | Lys | Glu | Lys | Leu | Thr | Ala | Asp | Pro | Asp | Ser | Glu | Val | Ala | 260 | 265 | 270 | |
| Thr | Thr | Ser | Leu | Pro | Gly | Val | Thr | His | Val | Pro | Ala | Arg | Lys | Met | Arg | 275 | 280 | 285 | |
| Leu | Thr | Val | Pro | Cys | Arg | Ala | Leu | Thr | Cys | Ala | His | Leu | Gln | Ser | Phe | 290 | 295 | 300 | |
| Asp | Ala | Ala | Leu | Tyr | Ile | Gln | Met | Asn | Glu | Lys | Lys | Pro | Thr | Trp | Thr | 305 | 310 | 315 | 320 |
| Cys | Pro | Val | Cys | Asp | Lys | Lys | Ala | Pro | Tyr | Glu | Ser | Leu | Ile | Ile | Asp | 325 | 330 | 335 | |
| Gly | Leu | Phe | Met | Glu | Ile | Leu | Asn | Ser | Cys | Ser | Asp | Cys | Asp | Glu | Ile | 340 | 345 | 350 | |
| Gln | Phe | Met | Glu | Asp | Gly | Ser | Trp | Cys | Pro | Met | Lys | Pro | Lys | Lys | Glu | 355 | 360 | 365 | |
| Ala | Ser | Glu | Val | Cys | Pro | Pro | Pro | Gly | Tyr | Gly | Leu | Asp | Gly | Leu | Gln | 370 | 375 | 380 | |
| Tyr | Ser | Ala | Val | Gln | Glu | Gly | Ile | Gln | Pro | Glu | Ser | Lys | Lys | Arg | Val | 385 | 390 | 395 | 400 |
| Glu | Val | Ile | Asp | Leu | Thr | Ile | Glu | Ser | Ser | Ser | Asp | Glu | Glu | Asp | Leu | 405 | 410 | 415 | |
| Pro | Pro | Thr | Lys | Lys | Gln | Cys | Ser | Val | Thr | Ser | Ala | Ala | Ile | Pro | Ala | 420 | 425 | 430 | |
| Leu | Leu | Gly | Ser | Lys | Gly | Val | Leu | Thr | Ser | Gly | His | Gln | Pro | Ser | Ser | 435 | 440 | 445 | |
| Val | Leu | Arg | Ser | Pro | Ala | Met | Gly | Thr | Leu | Gly | Ser | Asp | Phe | Leu | Ser | 450 | 455 | 460 | |
| Ser | Leu | Pro | Val | His | Glu | Tyr | Pro | Pro | Ala | Phe | Pro | Leu | Gly | Ala | Asp | 465 | 470 | 475 | 480 |
| Ile | Gln | Gly | Leu | Asp | Leu | Phe | Ser | Phe | Leu | Gln | Thr | Glu | Ser | Gln | Gln | 485 | 490 | 495 | |
| Tyr | Gly | Pro | Ser | Val | Ile | Ile | Ser | Leu | Asp | Glu | Gln | Asp | Thr | Leu | Gly | 500 | 505 | 510 | |
| His | Pro | Phe | Gln | Tyr | Arg | Gly | Thr | Pro | Ser | His | Phe | Leu | Gly | Pro | Leu | 515 | 520 | 525 | |

Ala Pro Thr Leu Gly Ser Cys His Gly Ser Ser Thr Pro Ala Pro Pro
530 535 540

Pro Gly Arg Val Ser Ser Ile Val Ala Pro Gly Ser Ser Leu Arg Glu
545 550 555 560

Gly His Gly Gly Pro Leu Pro Ser Gly Pro Ser Leu Thr Gly Cys Arg
565 570 575

Ser Asp Val Ile Ser Leu Asp
580

<210> 8

<211> 572

<212> PRT

<213> Homo sapiens

<400> 8

Met Ala Asp Phe Glu Glu Leu Arg Asn Met Val Ser Ser Phe Arg Val
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Ser Glu Leu Gln Val Leu Leu Gly Phe Ala Gly Arg Asn Lys Ser Gly
20 25 30

Arg Lys His Asp Leu Leu Met Arg Ala Leu His Leu Leu Lys Ser Gly
35 40 45

Cys Ser Pro Ala Val Gln Ile Lys Ile Arg Glu Leu Tyr Arg Arg Arg
50 55 60

Tyr Pro Arg Thr Leu Glu Gly Leu Ser Asp Leu Ser Thr Ile Lys Ser
65 70 75 80

Ser Val Phe Ser Leu Asp Gly Gly Ser Ser Pro Val Glu Pro Asp Leu
85 90 95

Ala Val Ala Gly Ile His Ser Leu Pro Ser Thr Ser Val Thr Pro His
100 105 110

Ser Pro Ser Ser Pro Val Gly Ser Val Leu Leu Gln Asp Thr Lys Pro
115 120 125

Thr Phe Glu Met Gln Gln Pro Ser Pro Pro Ile Pro Pro Val His Pro
130 135 140

Asp Val Gln Leu Lys Asn Leu Pro Phe Tyr Asp Val Leu Asp Val Leu
145 150 155 160

Ile Lys Pro Thr Ser Leu Val Gln Ser Ser Ile Gln Arg Phe Gln Glu
165 170 175

Lys Phe Phe Ile Phe Ala Leu Thr Pro Gln Gln Val Arg Glu Ile Cys
180 185 190

Ile Ser Arg Asp Phe Leu Pro Gly Gly Arg Arg Asp Tyr Thr Val Gln
195 200 205

Val Gln Leu Arg Leu Cys Leu Ala Glu Thr Ser Cys Pro Gln Glu Asp
 210 215 220
 Asn Tyr Pro Asn Ser Leu Cys Ile Lys Val Asn Gly Lys Leu Phe Pro
 225 230 235 240
 Leu Pro Gly Tyr Ala Pro Pro Pro Lys Asn Gly Ile Glu Gln Lys Arg
 245 250 255
 Pro Gly Arg Pro Leu Asn Ile Thr Ser Leu Val Arg Leu Ser Ser Ala
 260 265 270
 Val Pro Asn Gln Ile Ser Ile Ser Trp Ala Ser Glu Ile Gly Lys Asn
 275 280 285
 Tyr Ser Met Ser Val Tyr Leu Val Arg Gln Leu Thr Ser Ala Met Leu
 290 295 300
 Leu Gln Arg Leu Lys Met Lys Gly Ile Arg Asn Pro Asp His Ser Arg
 305 310 315 320
 Ala Leu Ile Lys Glu Lys Leu Thr Ala Asp Pro Asp Ser Glu Ile Ala
 325 330 335
 Thr Thr Ser Leu Arg Val Ser Leu Met Cys Pro Leu Gly Lys Met Arg
 340 345 350
 Leu Thr Ile Pro Cys Arg Ala Val Thr Cys Thr His Leu Gln Cys Phe
 355 360 365
 Asp Ala Ala Leu Tyr Ile Gln Met Asn Glu Lys Lys Pro Thr Trp Ile
 370 375 380
 Cys Pro Val Cys Asp Lys Lys Ala Ala Tyr Glu Ser Leu Ile Leu Asp
 385 390 395 400
 Gly Leu Phe Met Glu Ile Leu Asn Asp Cys Ser Asp Val Asp Glu Ile
 405 410 415
 Lys Phe Gln Glu Asp Gly Ser Trp Cys Pro Met Arg Pro Lys Lys Glu
 420 425 430
 Ala Met Lys Val Ser Ser Gln Pro Cys Thr Lys Ile Glu Ser Ser Ser
 435 440 445
 Val Leu Ser Lys Pro Cys Ser Val Thr Val Ala Ser Glu Ala Ser Lys
 450 455 460
 Lys Lys Val Asp Val Ile Asp Leu Thr Ile Glu Ser Ser Ser Asp Glu
 465 470 475 480
 Glu Glu Asp Pro Pro Ala Lys Arg Lys Cys Ile Phe Met Ser Glu Thr
 485 490 495
 Gln Ser Ser Pro Thr Lys Gly Val Leu Met Tyr Gln Pro Ser Ser Val
 500 505 510

Arg Val Pro Ser Val Thr Ser Val Asp Pro Ala Ala Ile Pro Pro Ser
515 520 525

Leu Thr Asp Tyr Ser Val Pro Phe His His Thr Pro Ile Ser Ser Met
530 535 540

Ser Ser Asp Leu Pro Gly Glu Gln Arg Phe Asn Asp Ile Asn Asn Glu
545 550 555 560

Leu Lys Leu Gly Thr Ser Ser Asp Thr Val Gln Gln
565 570

<210> 9

<211> 621

<212> PRT

<213> Homo sapiens

<400> 9

Met Ala Asp Phe Glu Glu Leu Arg Asn Met Val Ser Ser Phe Arg Val
1 5 10 15

Ser Glu Leu Gln Val Leu Leu Gly Phe Ala Gly Arg Asn Lys Ser Gly
20 25 30

Arg Lys His Asp Leu Leu Met Arg Ala Leu His Leu Leu Lys Ser Gly
35 40 45

Cys Ser Pro Ala Val Gln Ile Lys Ile Arg Glu Leu Tyr Arg Arg Arg
50 55 60

Tyr Pro Arg Thr Leu Glu Gly Leu Ser Asp Leu Ser Thr Ile Lys Ser
65 70 75 80

Ser Val Phe Ser Leu Asp Gly Gly Ser Ser Pro Val Glu Pro Asp Leu
85 90 95

Ala Val Ala Gly Ile His Ser Leu Pro Ser Thr Ser Val Thr Pro His
100 105 110

Ser Pro Ser Ser Pro Val Gly Ser Val Leu Leu Gln Asp Thr Lys Pro
115 120 125

Thr Phe Glu Met Gln Gln Pro Ser Pro Pro Ile Pro Pro Val His Pro
130 135 140

Asp Val Gln Leu Lys Asn Leu Pro Phe Tyr Asp Val Leu Asp Val Leu
145 150 155 160

Ile Lys Pro Thr Ser Leu Val Gln Ser Ser Ile Gln Arg Phe Gln Glu
165 170 175

Lys Phe Phe Ile Phe Ala Leu Thr Pro Gln Gln Val Arg Glu Ile Cys
180 185 190

Ile Ser Arg Asp Phe Leu Pro Gly Gly Arg Arg Asp Tyr Thr Val Gln
195 200 205

| | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Gln | Leu | Arg | Leu | Cys | Leu | Ala | Glu | Thr | Ser | Cys | Pro | Gln | Glu | Asp | 210 | 215 | 220 |
| Asn | Tyr | Pro | Asn | Ser | Leu | Cys | Ile | Lys | Val | Asn | Gly | Lys | Leu | Phe | Pro | 225 | 230 | 235 |
| Leu | Pro | Gly | Tyr | Ala | Pro | Pro | Pro | Lys | Asn | Gly | Ile | Glu | Gln | Lys | Arg | 245 | 250 | 255 |
| Pro | Gly | Arg | Pro | Leu | Asn | Ile | Thr | Ser | Leu | Val | Arg | Leu | Ser | Ser | Ala | 260 | 265 | 270 |
| Val | Pro | Asn | Gln | Ile | Ser | Ile | Ser | Trp | Ala | Ser | Glu | Ile | Gly | Lys | Asn | 275 | 280 | 285 |
| Tyr | Ser | Met | Ser | Val | Tyr | Leu | Val | Arg | Gln | Leu | Thr | Ser | Ala | Met | Leu | 290 | 295 | 300 |
| Leu | Gln | Arg | Leu | Lys | Met | Lys | Gly | Ile | Arg | Asn | Pro | Asp | His | Ser | Arg | 305 | 310 | 315 |
| Ala | Leu | Ile | Lys | Glu | Lys | Leu | Thr | Ala | Asp | Pro | Asp | Ser | Glu | Ile | Ala | 325 | 330 | 335 |
| Thr | Thr | Ser | Leu | Arg | Val | Ser | Leu | Met | Cys | Pro | Leu | Gly | Lys | Met | Arg | 340 | 345 | 350 |
| Leu | Thr | Ile | Pro | Cys | Arg | Ala | Val | Thr | Cys | Thr | His | Leu | Gln | Cys | Phe | 355 | 360 | 365 |
| Asp | Ala | Ala | Leu | Tyr | Ile | Gln | Met | Asn | Glu | Lys | Lys | Pro | Thr | Trp | Ile | 370 | 375 | 380 |
| Cys | Pro | Val | Cys | Asp | Lys | Lys | Ala | Ala | Tyr | Glu | Ser | Leu | Ile | Leu | Asp | 385 | 390 | 395 |
| Gly | Leu | Phe | Met | Glu | Ile | Leu | Asn | Asp | Cys | Ser | Asp | Val | Asp | Glu | Ile | 405 | 410 | 415 |
| Lys | Phe | Gln | Glu | Asp | Gly | Ser | Trp | Cys | Pro | Met | Arg | Pro | Lys | Lys | Glu | 420 | 425 | 430 |
| Ala | Met | Lys | Val | Ser | Ser | Gln | Pro | Cys | Thr | Lys | Ile | Glu | Ser | Ser | Ser | 435 | 440 | 445 |
| Val | Leu | Ser | Lys | Pro | Cys | Ser | Val | Thr | Val | Ala | Ser | Glu | Ala | Ser | Lys | 450 | 455 | 460 |
| Lys | Lys | Val | Asp | Val | Ile | Asp | Leu | Thr | Ile | Glu | Ser | Ser | Ser | Asp | Glu | 465 | 470 | 475 |
| Glu | Glu | Asp | Pro | Pro | Ala | Lys | Arg | Lys | Cys | Ile | Phe | Met | Ser | Glu | Thr | 485 | 490 | 495 |
| Gln | Ser | Ser | Pro | Thr | Lys | Gly | Val | Leu | Met | Tyr | Gln | Pro | Ser | Ser | Val | 500 | 505 | 510 |

Arg Val Pro Ser Val Thr Ser Val Asp Pro Ala Ala Ile Pro Pro Ser
 515 520 525
 Leu Thr Asp Tyr Ser Val Pro Phe His His Thr Pro Ile Ser Ser Met
 530 535 540
 Ser Ser Asp Leu Pro Gly Leu Asp Phe Leu Ser Leu Ile Pro Val Asp
 545 550 555 560
 Pro Gln Tyr Cys Pro Pro Met Phe Leu Asp Ser Leu Thr Ser Pro Leu
 565 570 575
 Thr Ala Ser Ser Thr Ser Val Thr Thr Thr Ser Ser His Glu Ser Ser
 580 585 590
 Thr His Val Ser Ser Ser Ser Ser Arg Ser Glu Thr Gly Val Ile Thr
 595 600 605
 Ser Ser Gly Ser Asn Ile Pro Glu Ile Ile Ser Leu Asp
 610 615 620

<210> 10
 <211> 510
 <212> PRT
 <213> Homo sapiens

<400> 10
 Met Ala Ala Glu Leu Val Glu Ala Lys Asn Met Val Met Ser Phe Arg
 1 5 10 15
 Val Ser Asp Leu Gln Met Leu Leu Gly Phe Val Gly Arg Ser Lys Ser
 20 25 30
 Gly Leu Lys His Glu Leu Val Thr Arg Ala Leu Gln Leu Val Gln Pro
 35 40 45
 Asp Cys Ser Pro Glu Leu Phe Lys Lys Ile Lys Glu Leu Tyr Glu Thr
 50 55 60
 Arg Tyr Ala Lys Lys Asn Ser Glu Pro Ala Pro Gln Pro His Arg Pro
 65 70 75 80
 Leu Asp Pro Leu Thr Met His Ser Thr Tyr Asp Arg Ala Gly Ala Val
 85 90 95
 Pro Arg Thr Pro Leu Ala Gly Phe Asn Ile Asp Tyr Pro Val Leu Tyr
 100 105 110
 Gly Lys Tyr Leu Asn Gly Leu Gly Arg Leu Pro Ala Lys Thr Leu Lys
 115 120 125
 Pro Glu Val Arg Leu Val Lys Leu Pro Phe Phe Asn Met Leu Asp Glu
 130 135 140
 Leu Leu Lys Pro Thr Glu Leu Val Pro Gln Asn Asn Glu Lys Leu Gln
 145 150 155 160

Glu Ser Pro Cys Ile Phe Ala Leu Thr Pro Arg Gln Val Glu Leu Ile
 165 170 175
 Arg Phe Lys Gln Gly Met Gln Pro Gly Val Lys Ala Val Gln Val Val
 180 185 190
 Leu Arg Ile Cys Tyr Ser Asp Thr Ser Cys Pro Gln Glu Asp Gln Tyr
 195 200 205
 Pro Pro Asn Ile Ala Val Lys Val Asn His Ser Tyr Cys Ser Val Pro
 210 215 220
 Gly Tyr Tyr Pro Ser Asn Lys Pro Gly Val Glu Pro Lys Arg Pro Cys
 225 230 235 240
 Arg Pro Ile Asn Leu Thr His Leu Met Tyr Leu Ser Ser Ala Thr Asn
 245 250 255
 Arg Ile Thr Val Thr Trp Gly Asn Tyr Gly Lys Ser Tyr Ser Val Ala
 260 265 270
 Leu Tyr Leu Val Arg Gln Leu Thr Ser Ser Glu Leu Leu Gln Arg Leu
 275 280 285
 Lys Thr Ile Gly Val Lys His Pro Glu Leu Cys Lys Ala Leu Val Lys
 290 295 300
 Glu Lys Leu Arg Leu Asp Pro Asp Ser Glu Ile Ala Thr Thr Gly Val
 305 310 315 320
 Arg Val Ser Leu Ile Cys Pro Leu Val Lys Met Arg Leu Ser Val Pro
 325 330 335
 Cys Arg Ala Glu Thr Cys Ala His Leu Gln Cys Phe Asp Ala Val Phe
 340 345 350
 Tyr Ile Gln Met Asn Glu Lys Lys Pro Thr Trp Met Cys Pro Val Cys
 355 360 365
 Asp Lys Pro Ala Pro Tyr Asp Gln Leu Ile Ile Asp Gly Leu Leu Ser
 370 375 380
 Lys Ile Leu Ser Glu Cys Glu Asp Ala Asp Glu Ile Glu Tyr Leu Val
 385 390 395 400
 Asp Gly Ser Trp Cys Pro Ile Arg Ala Glu Lys Glu Arg Ser Cys Ser
 405 410 415
 Pro Gln Gly Ala Ile Leu Val Leu Gly Pro Ser Asp Ala Asn Gly Leu
 420 425 430
 Leu Pro Ala Pro Ser Val Asn Gly Ser Gly Ala Leu Gly Ser Thr Gly
 435 440 445
 Gly Gly Gly Pro Val Gly Ser Met Glu Asn Gly Lys Pro Gly Ala Asp
 450 455 460

Val Val Asp Leu Thr Leu Asp Ser Ser Ser Ser Ser Glu Asp Glu Glu
465 470 475 480

Glu Glu Glu Glu Glu Glu Glu Asp Glu Asp Glu Glu Gly Pro Arg Pro
485 490 495

Lys Arg Arg Cys Pro Phe Gln Lys Gly Leu Val Pro Ala Cys
500 505 510